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The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 35

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte HARRIHAR A. PERSHADSINGH
and THEODORE W. KURTZ

Appeal No. 95-0885
Application 07/725,327¹

HEARD: OCTOBER 14, 1997

Before JOHN D. SMITH, GARRIS and WEIFFENBACH, *Administrative Patent Judges*.

WEIFFENBACH, *Administrative Patent Judge*.

DECISION ON APPEAL

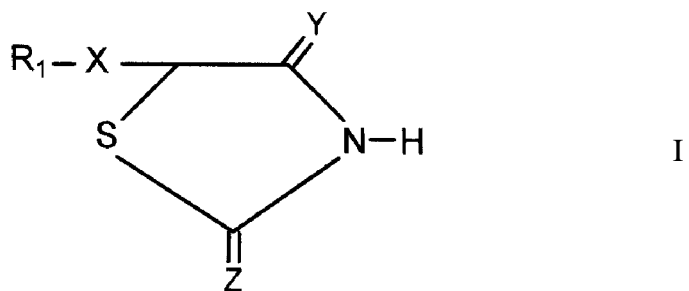
This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-7 and 9-18. We affirm-in-part.

¹ Application for patent filed July 8, 1991. According to applicants, this Application is a continuation-in-part of Application 07/421,102, filed October 13, 1989, now U.S. Patent No. 5,053,420, granted October 1, 1991.

The Claimed Subject Matter

The claims on appeal are directed to a method for controlling *essential hypertension* and its related cardiovascular syndrome in a mammalian host. Claims 1 and 18 are illustrative of subject matter appellants regard as their invention:

1. A method for controlling essential hypertension and its related cardiovascular syndrome in a mammalian host in need thereof by administration of an effective amount of a 5-aryl substituted thiazolidine derivative of formula I



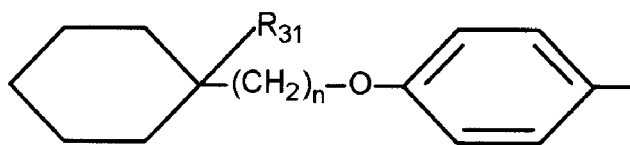
where: R_1 is an aromatic carbocyclic or an aromatic heterocyclic;

X is a lower alkylidene or a bond; or $-HC=CH-$

Y is oxo or imino;

Z is oxo or imino;

and pharmaceutically acceptable salts thereof with the proviso that R_1 is not of the formula



where n is 1-4, and where R_{31} is hydrogen or lower alkyl or 1-4 carbons and the cyclohexane ring may be optionally substituted at any available methylene with single oxo or hydroxy.

18. The method of claim 1 wherein the thiazolidine derivative is 5-{4-[2-(5-ethyl-2-pyridyl)ethoxy]benzyl}-2,4-thiazolidine dione.

The Prior Art

The following prior art reference is relied upon by the examiner in support of the rejection of obviousness:

Hindley

5,002,953

Mar. 26, 1991
(parent filed Aug. 30, 1988)

Hindley discloses a substituted-thiazolidinedione derivative. The patentee discloses the following at col. 1, lines 19-29:

It has now surprisingly been discovered that certain novel substituted-thiazolidinedione derivatives show improved blood-glucose lowering activity and are therefore of potential use in the treatment and/or prophylaxis of hyperglycaemia and are of particular use in the treatment of Type II diabetes.

These compounds are also indicated to be of potential use for the treatment and/or prophylaxis of other diseases including hyperlipidaemia, hypertension, cardiovascular disease and certain eating disorders.

The Rejection²

Claims 1-7 and 9-18 stand rejected under 35 U.S.C. § 103 as being unpatentable over Hindley.³ According to the examiner, Hindley “clearly suggests the use of applicant’s claimed composition to be used to treat hypertension” (answer, p. 3).

Grouping of Claims

Appellants submit at page 1 of their brief that the appealed claims do not stand or fall together. Claims 2-7 and 9-18 are dependent claims which are ultimately dependent on independent claim 1. Appellants point out that the “elected species reads on claims 1, 2, 3, 4, 5 and 18” and that the “remaining pending claims (claims 6, 7, and 9-17) claim genera distinct from the genus of the elected species” (brief, p. 1). On page 18 of the brief, appellants state that they

... wish to point out that the thiazolidine derivatives utilized in the claimed methods include species that are structurally distinct from the compounds of Hindley. For

² In the final rejection (Paper No. 15), claims 1-17 were rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement and under 35 U.S.C. § 101 for lack of demonstrated utility. Both rejections have been withdrawn by the examiner. See the advisory action dated December 8, 1993 (Paper No. 19).

³ Claims 1-17 were rejected under 35 U.S.C. § 103 over Hindley. In an amendment after final (Paper No. 22), claim 8 was cancelled and new claim 18 was added. In the advisory action (Paper No. 23), after the examiner advised appellants that the amendment would be entered and noted that the status of the claims remained the same, i.e. claims 1-17 were rejected. The examiner did not state the status of new claim 18. However, in the brief, appellants appear to understand that the claims under rejection are claims 1-7 and 9-18 (brief, p. 1, ¶ I) and the examiner agreed (answer, p. 1, ¶ 1). Accordingly, we consider that the rejection before us includes claim 18.

example, appellants draw the Board's attention to the structural differences between the elected species (see, e.g., claim 18) and the compounds disclosed in Hindley. The Hindley compounds are limited to primary and secondary amino compounds ...

Other than claim 18, appellants have not presented arguments in their brief specifically arguing the separate patentability of any other dependent claim over the prior art as required by 37 CFR §§ 1.192(c)(5) and (c)(6)(iv) (1993). Accordingly, dependent claim 18 will stand or fall on its own and dependent claims 2-7 and 9-17 will stand or fall independent claim 1. *In re Nielson*, 816 F.2d 1567, 1571, 2 USPQ2d 1525, 1527 (Fed. Cir. 1987); *In re Wood*, 582 F.2d 638, 642, 199 USPQ 137, 140 (CCPA 1978); *Ex parte Schier*, 21 USPQ2d 1016, 1081 (Bd. Pat. App. & Int. 1991).

Opinion

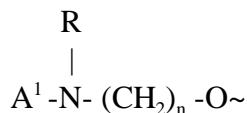
We have carefully considered the respective positions advanced by appellants and the examiner. For the reasons set forth below, we will affirm-in-part the examiner's rejection of the appealed claims for obviousness under 35 U.S.C. § 103.

Appellants argue, with regard to claim 18, that the thiazolidine derivative claimed therein includes a specie that is structurally distinct from the compounds of Hindley. Appellants point to the fact that Hindley's compounds are limited to primary and secondary amino compounds. In response, the examiner asserts that

[a]ppellants argue for the first time that their active agents differ from the Hindley compounds. This argument is not persuasive as there is no evidence of record which establishes the unpredictability of the resulting effect. [Answer, p. 4.]

The burden is on the examiner to establish a *prima facie* case of obviousness, in this case establishing that the claimed compounds would have been structurally obvious over Hindley's compounds. It is

evident that Hindley's compounds include a primary or secondary amine component comprising:



where R can be hydrogen or an alkyl or aryl group and A¹ is a substituted or unsubstituted aromatic heterocyclic group. The amine component is conspicuously missing from the compounds defined in appellants' dependent claim 18. Since the examiner has not presented any reasoning as to why the compounds in the claims on appeal would be structurally obvious over Hindley, the rejection as to claim 18 is reversed.

Claim 1 is directed to a method of controlling *essential hypertension* using a thiazolidine derivative. Claim 1 defines a compound having a 5-aryl substituted thiazolidine component of formula I wherein R₁ is an aromatic carbocyclic or an aromatic heterocyclic, X can be a lower alkylidene radical, and Y and Z can be oxo. In the specification, appellants define "carbocyclic" as being "a homocyclic ring compound in which all the ring atoms are carbon, e.g. benzene" (p. 15, lines 36-37), "heterocyclic" as being a "ring compound having atoms other than carbon in its nucleus, e.g. pyrrole or thiophene (p. 16, lines 1-3), and "benzyl" as "an aryl radical derived from toluene" (p. 16, lines 12-13).

Hindley does disclose thiazolidinedione compounds having the thiazolidine component of formula I as set forth in appellants' claims (where X is a lower alkyl group, and Y and Z are oxo) to which is linked or bridged an aromatic carboxylic (see *inter alia*, Examples 1, 5, 7 and 11 in Hindley) and aromatic heterocyclic components (see *inter alia*, Examples 3, 7, 10, 19 and 23). Accordingly,

we agree with the examiner that Hindley teaches closely related compounds possessing the thiazolidine moiety as claimed by appellants.

The examiner concluded that the compounds recited in claim 1 would have been obvious over Hindley because the patentee discloses thiazolidine derivatives that can be used to treat hypertension. Appellants' principal argument is that Hindley's hypertension is not *essential hypertension* as required by the claims on appeal. Appellants contend that those skilled in the art would have recognized that hypertension is not synonymous with *essential hypertension*, that there is no reasonable expectation that thiazolidines would be useful to treat *essential hypertension*, and that, at best, Hindley provides an invitation to experiment. Appellants argue that "where Hindley refers to 'hyperlipidemia, hypertension, cardiovascular disease, and certain eating disorders' one of ordinary skill would understand this to be a suggestion that treatment of diabetes with thiazolidines may also be useful to ameliorate the signs and symptoms that are secondary to the diabetes" (brief, p. 9). Appellants rely on declarations by Dr. Kurtz, M.D. (hereinafter the Kurtz I declaration⁴), one of the named inventors, and a declaration by Dr. Mark, M.D. (the Mark declaration) to support their arguments.

Both the Mark and Kurtz I declarations state that "[e]ssential hypertension is a specifically diagnosed clinical disorder and hypertension is a 'sign' [symptom] of many other clinical disorders" (Mark declaration, ¶6(a) and Kurtz I declaration, ¶5(a)). Appellants define *essential hypertension*

⁴ Two declarations were submitted by Dr. Kurtz during prosecution. One declaration (the Kurtz I declaration) was submitted on July 2, 1993 and assigned Paper No. 14. The other declaration (the Kurtz II declaration) was submitted on November 23, 1993 and assigned Paper No. 18. The Kurtz II declaration is not relevant to our decision here since it is directed to an interpretation of the Kotchen, Meehan and Fujiwara references which are not before us.

in their specification as being hypertension of unknown etiology (specification, p. 1, lines 11 and 12). Appellants did not define the meaning of “hypertension”. It would appear from the Mark and Kurtz I declarations that hypertension is everything which “essential hypertension” is not. *Stedman’s Medical Dictionary* defines “hypertension” follows:⁵

hypertension (hi’per-ten’shun) [hyper- + L. *tensio*, tension]. High blood pressure.

adrenal h., h. due to a pheochromocytoma.

benign h., essential h. that runs a relatively long and symptomless course.

essential h., hyperpiesis; primary h.; idiopathic h.; h. without preexisting renal disease or unknown cause.

Goldblatt’s h., Goldblatt *phenomenon*.

idiopathic h., essential h.

malignant h., severe h. that runs a rapid course, causing necrosis of arteriolar walls in kidney, retina, etc. Hemorrhages occur, and death most frequently is caused by uremia or rupture of a cerebral vessel.

pale h., h. with pallor of the skin, a severe form with pronounced constriction of peripheral vessels.

portal h., h. in the portal system as seen in cirrhosis of the liver and other conditions causing obstruction to the portal vein.

postpartum h., increased tension or blood pressure during the six weeks immediately following the completion of labor.

primary h., essential h.

pulmonary h., h. in the pulmonary circuit; It may be primary, or secondary to pulmonary or cardiac disease, e.g., fibrosis of the lung or mitral stenosis.

renal h., h. secondary to renal disease.

renovascular h., h. produced by renal arterial obstruction.

It is clear from *Steadman’s* definition that “hypertension” is a generic term and encompasses “essential hypertension.” Thus, the terms are distinct, but only to the extent that “hypertension” is

⁵ *Steadman’s Medical Dictionary*, 24th Edition, Williams & Wilkins, Baltimore, Maryland, pages 676-77 (1982). A copy is attached to this decision.

generic to “essential hypertension.” Considering the term “hypertension” in the context of its ordinary meaning, we find that Hindley’s “hypertension” would include “*essential hypertension*.”

Both Mark and Kurtz I in their separate declarations set forth three reasons “why one of skill would have no reason to expect that essential hypertension is treatable with thiazolidines after reading the Hindley patent” (Mark declaration, ¶6(b) and Kurtz I declaration, ¶5(a)). First, Hindley is primarily directed to the use of thiazolidines to treat diabetes and therefore one skilled in the art would read Hindley as treating other diseases associated with Type II diabetes, including hypertension, cardiovascular disease such as vascular occlusions, and eating disorders such as hyperphagia (overeating) or polydipsia (excessive thirst). Second, if one reads Hindley as treating the general “sign” of hypertension, the reference is meaningless outside the context of diabetes because the reference would be suggesting a treatment for hundreds of different clinical disorders with no guidance to the medical doctor for using the Hindley’s compound to treat a specific disorder. The Mark declaration points out further that drugs effective for secondary hypertension conditions such as glucocorticoid remediable aldosteronism can “dangerously exacerbate essential hypertension.” Third, one skilled in the art would not have a reasonable expectation that Hindley’s compound would be effective against “*essential hypertension*” because the etiology of *essential hypertension* is complex and involves multiple factors such as insulin resistance, impaired renal function, excess sympathetic nervous system activity, excess salt intake, and insufficient potassium intake. Because of these multiple factors, one skilled in the art would not have been led to conclude with a reasonable degree of certainty that Hindley’s thiazolidines would be useful to treat “*essential hypertension*.”

We do not find these reasons persuasive. We find, for reasons already given, that the ordinary meaning of the term “hypertension” would include “*essential hypertension*.” Moreover, Hindley does not qualify his reference to “other diseases” as being limited to only those diseases associated with Type II diabetes or hyperglycemia. In view of the definition of “hypertension” *supra*, we find nothing in the context of Hindley’s disclosure which would have lead one skilled in the art to such a limited interpretation. Even assuming that one skilled in the art would have interpreted Hindley as being limited to hypertension associated with Type II diabetes or hypoglycemia, neither appellants nor the declarants have presented any evidence which would lend support for such an interpretation. Hindley specifically discloses that his compounds can be used to treat hypertension, cardiovascular disease and certain eating disorders (col. 9, lines 55-60) and that the “dosage regimens for the treatment of hypertension, cardiovascular disease and eating disorders will generally be those mentioned ... in relation to hyperglycemia” (col. 11, lines 6-9). We conclude that Hindley would have reasonably suggested to one having ordinary skill in the art to expect that the disclosed thiazolidinedione derivatives would be useful to treat “*essential hypertension*.” Obviousness does not require absolute predictability, but only the reasonable expectation of success. *In re Clinton*, 527 F. 2d 1226, 1228, 188 USPQ 365, 367 (CCPA 1976); *In re Kronig*, 539 F.2d 1300, 1304, 190 USPQ 425, 428 (CCPA 1976); *In re Lamberti*, 545 F.2d 747, 750, 192 USPQ 278, 280 (CCPA 1976).

Accordingly, for the foregoing reasons we conclude that the examiner has made out a *prima facie* case of obviousness over Hindley as to claims 1-7 and 9-17 because it is reasonable over the teachings of Hindley that one skilled in the art would have had a reasonable expectation of success

that Hindley's compounds and derivatives would alleviate *essential hypertension*. We find no evidence of record which would rebut the *prima facie* case. *In re Hedges*, 783 F.2d 1038, 1041, 228 USPQ 685, 687 (Fed. Cir. 1986); *In re Piasecki*, 745 F.2d 1468, 1471-1473, 223 USPQ 785, 787-788 (Fed. Cir. 1984).

Conclusion

For the reasons given above, the rejection of claims 1-7 and 9-17 for obviousness over Hindley is affirmed while the rejection of claim 18 over Hindley is reversed. Accordingly, the decision of the examiner is affirmed-in-part.

AFFIRMED-IN-PART

JOHN D. SMITH)
Administrative Patent Judge)
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Appeal No. 95-0885
Application 07/725,327

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)	APPEALS AND
BRADLEY R. GARRIS)	INTERFERENCES
Administrative Patent Judge)	
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CAMERON WEIFFENBACH)	
Administrative Patent Judge)	

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